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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,179	12/09/2005	Shigeru Akasofu	09857/0203535-US0	7982

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EXAMINER	
CLAYTOR, DEIRDRE RENEE	

ART UNIT	PAPER NUMBER
1617	

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01/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,179	AKASOFU ET AL.	
	Examiner	Art Unit	
	Renee Claytor	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/30/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

Applicants response filed on 10/30/2007 is acknowledged. Applicants have cancelled claims 1-12, 14-17 and 19-27. Currently claims 13 and 18 are under examination.

Applicants have amended the claims to overcome the claim objections and it is hereby withdrawn.

Applicant's arguments over the 35 USC 112 rejection have been fully considered. In particular, Applicants argue that the specification discloses experiments wherein the claimed compound provides a protective effect to neurons from injury and point to specific examples beginning on page 22 of the specification. In addition, Applicants argue over the second 35 USC 112 rejection that it was not clear to the Examiner what neurons were being protected from in claim 13 as previously written and the word "protection" was interpreted to mean "prevention". Applicants argue that protection of neurons relates to reducing the severity of neuron damage.

In response to the above arguments, the Examiner notes that the examples in the specification show that donepezil decreases Aβ aggregation in cholinergic neurons (focusing on the elected species) but nowhere is it taught that there is a prevention of damage induced by Aβ aggregation. The Examiner is still taking the interpretation of "protection" to mean "prevention". Though Applicants argue that protection of neurons relates to reducing the severity of neuron damage, the Examiner would like to point out that the specification teaches that "protection of neurons include not only to actually

prevent the death of neurons of the central nervous system..." (see pages 41, lines 5-10). Accordingly, the claims are being treated as they read on prevention and the 35 USC 112, first paragraph rejection is maintained. Because Applicants have amended claim 13 to further explain what the neurons are being "protected" from, the 35 USC 112, second paragraph rejection is withdrawn.

Applicant's arguments over the 35 USC 102 rejection have been fully considered. Applicants argue that Emilien discloses that donepezil was approved as a symptomatic therapy for mild to moderate AD and does not expressly disclose the protection of neurons from damage induced by cerebral ischemia, excitotoxicity, Aβ toxicity, or Aβ aggregation.

This argument is not found persuasive because as discussed in the rejection, it is well known in the art, and is taught by Michaelis that the generation, aggregation and deposition of Aβ plaques is associated with AD. Accordingly, because it is known in the art that donepezil treats AD, there would be an overlapping patient population because AD is associated with deposition of Aβ plaques as well as the cholinergic system. Inherently, donepezil would inherently treat neurons in the treatment of AD.

Claim Rejections – 35 U.S.C. §112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13 and 18 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating Aβ aggregation in cholinergic neurons in the CNS, does not reasonably provide enablement for protecting (interpreted by the Examiner to mean prevention) all neurons of the CNS. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

1) The nature of the invention and breadth of the claims: The nature of the invention and breadth of the claims are drawn to a method of protecting neurons of the central nervous system, comprising administration of donepezil.

2) The presence or absence of working examples and the amount of direction or guidance presented: In the instant case, no working examples are presented in the specification as filed showing how to prevent Aβ aggregation in

cholinergic neurons. The specification outlines experiments showing that donepezil decreases Aβ aggregation in cholinergic neurons. Figures 8-10 shows that the addition of donepezil decreases Aβ aggregation in cholinergic neurons, proving that donepezil is effective at reducing Aβ aggregation and not for prevention of Aβ aggregation.

3) The state of the prior art: The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more details as to how to make and use invention in order to be enabling. >See, e.g., Chiron Corp. v. Genentech Inc., 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004).

The state of the art regarding treating Aβ aggregation in PC12 shows that administration of donepezil decreases Aβ toxicity (see Figure 1) but does not show total inhibition on toxicity induced by Aβ (see NeuroReport (1998) 9, 1519-1522). Therefore, the use of donepezil is not art recognized as preventing Aβ toxicity.

4) The quantity of experimentation necessary: Claims 13 and 18 read on a method of protecting neurons of the central nervous system, comprising administration of donepezil. As discussed above, the specification fails to provide sufficient support for completely preventing disorders, such as Aβ toxicity in neurons. Applicant fails to

provide information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Claim Rejections – 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13 and 18 rejected under 35 U.S.C. 102(b) as being anticipated by Emilien et al. (Arch Neurol 57 (2000) pgs. 454- 459) as evidenced by Michaelis (JPET 304 (2003) 897-904).

Emilien et al. teach that 1-benzy-4-L(5,6-dimethyloxy-1-indanone)-2-yl]methylpiperidine (herein after termed donepezil) is an acetylcholinesterase, FDA approved therapy for Alzheimer's disease (see pg. 455, Col. 2).

The treatment of a disorder in a neuron that is induced by Aβ toxicity is inherently taught by Emilien et al. According to Michaelis the generation, aggregation and deposition of amyloid (Aβ) plaques in the brain is associated with Alzheimer's disease in the brain (pg. 898, first paragraph in second column). Aggregation of Aβ in the vicinity

of neurons leads to toxic cellular events and is regarded as the culprit responsible for neurodegeneration (pg. 900, first paragraph in first column; pg. 901, second paragraph in first column). Therefore, because donepezil treats Alzheimer's, it would necessarily treat Aβ toxicity as well.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Renee Claytor whose telephone number is 571-272-8394. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

RC

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER